REMARKS/ARGUMENTS

The claims are 1-23. Claims 2 and 14 have been amended to better define the invention. In particular, claims 2 and 14 have been rewritten in independent form to incorporate the subject matter of claims 1 and 13, respectively. Support for the amendments to claims 2 and 14 may be found, *inter alia*, in claims 1 and 13 as filed and in the disclosure at page 11, second full paragraph, and at pages 15-16. Reconsideration is expressly requested.

Claims 1, 2, 4, 7-9, 11-16 and 19-20 were rejected under 35 U.S.C. 103(a) as being unpatentable over *U.S. Patent No. 6,223,069 to Pfeiffer et al.*, in view of U.S. Patent No. 6,339,714 6 to *Chen*. The remaining claims 3, 5, 6, 10, 17, 18 and 21-23 were rejected under 35 U.S.C. 103(a) as being unpatentable over *Pfeiffer et al* and *Chen* and further in view of *U.S. Patent No. 6,516,214 to Boas*.

Essentially the Examiner's position was that *Pfeiffer et al.* discloses the device for measuring cerebral blood flow in an organ using an injected indicator recited in the claims except

for delineating that the signal is divided into pulsatile and nonpulsatile components, that *Chen* discloses this feature, and that it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate this feature into *Pfeiffer et al.* for the purpose of obtaining the attenuation purely due to arterial blood. *Boas* was cited with respect to claims 3, 5, 6, 10, 17, 18 and 21-23 as teaching the use of a threshold value for comparison purposes and extrapolation of data for determining location.

The rejections are respectfully traversed.

As set forth in independent claims 1 and 13, Applicants' invention provides a device and a method, respectively, for measuring blood flow in an organ using an injected indicator. As recited in claim 1, the device includes a radiation source for emitting near infrared radiation into tissue of the organ at a first location, a sensor for detecting a proportion of the emitted near infrared radiation that exits from the organ at a second location, and an evaluation unit that detects the proportion of the emitted near infrared radiation that exits from tissue of the organ as an input signal. The input signal

contains a pulsatile component and a non-pulsatile component, and the evaluation unit is programmed to perform the following evaluation steps:

(a) dividing up the input signal into the pulsatile component and the non-pulsatile component;

(b) determination of injected indicator concentration with reference to the organ tissue from the non-pulsatile component of the input signal;

(c) iterative determination of an inflow function i(t) that characterizes blood flow through the organ by incrementally varying a mean transit time mtt until a stop criterion is reached;

(d) determination of injected indicator concentration with reference to blood volume in the organ from the pulsatile component of the input signal and the iteratively determined inflow function i(t);

(e) calculation of blood volume in the organ as a quotient of the injected indicator concentration with reference to the organ tissue and the injected indicator concentration with reference to the blood volume in the organ; and

(f) calculation of the blood flow in the organ as a quotient of the blood volume in the organ and the mean transit time mtt when the stop criterion has been reached.

These steps (a)-(f) are also recited in method claim 13. Claims 2 and 14, which have been amended to be in independent form, incorporate the subject matter of claims 1 and 13, respectively, and further recite scaling the inflow function i(t) by means of values determined from the pulsatile component of the input signal.

None of the cited references discloses or suggests the device and method as recited in claims 1 and 13. The references also fail to teach the benefits that result from the device and method as recited in Applicants' claims 1 and 13. These benefits include:

- the measuring of a single signal with respect to the organ under observation;
- the determination of organ blood flow and blood volume with respect to the organ under observation from the single signal;

- the ability to cancel all scattering and reflecting losses since the measured values are absolute because they are determined form a single signal;

- the reduction in the number of light sources and photodetectors; and

- the elimination of the error of determining surge time in the obtained values.

Pfeiffer et al. (US 6,223,069) discloses a process and device for non-invasive measurement of cerebral blood flow. The process and device simultaneously determine a blood flow index, which is directly proportional to the blood flow. A device for carrying out the process according to *Pfeiffer et al.* consists of a multichannel apparatus having at least two near-infrared spectroscopes, each having two pulsed monochromatic light sources with a measurement and a reference wavelength, respectively.

In the device according to *Pfeiffer et al.*, a non-invasive measuring device determines the concentration of the tracer in the arterial blood flow by pulse densitometry. A cerebral dye curve c(t) and an arterial dye curve a(t) are measured independently at the subject's head with at least two infrared spectroscopes and at the subject's finger with an additional non-invasive measuring device See *Pfeiffer et al.*, FIGS. 1A and

1B). A transcerebral transport function g(t), which expresses the correlation between a(t) and c(t), is determined by the development of a(t) and c(t) (See *Pfeiffer et al.*, column 4, line 60 to column 5, line 15). The blood flow index is calculated as the quotient of the maximum of g(t) and the surge time from 10% to 90% of the maximum of g(t) (See *Pfeiffer et al.*, column 7, lines 13-32). The relative cerebral blood volume according to *Pfeiffer et al.* is calculated as the product of the average transit time (mtt) of transport function g(t) and the relative blood flow index (See *Pfeiffer et al.*, column 8, line 13-15).

Applicants' claim 1 recites a device for measuring blood flow in an organ using injected indicator. The device as recited in Applicants' claim 1 includes a radiation source for emitting near infrared radiation into tissue of the organ at a first location and a sensor for detecting a proportion of the emitted near infrared radiation that exits form tissue of the organ at a second location. The detected input signal consists of a pulsatile and non-pulsatile component.

In the device recited in Applicants' claim 1, an evaluation unit divides the input signal into the pulsatile and

non-pulsatile components. The evaluation unit further carries out the following steps:

- determining the injected indicator concentration with reference to the organ tissue from the non-pulsatile component of the input signal;
- iteratively determining an inflow function i(t) that characterizes blood flow through the organ by incrementally varying a mean transit time mtt until a stop criterion is reached;
- determining the injected indicator concentration with reference to blood volume in the organ from the pulsatile component of the input signal and the iteratively determined inflow function i(t);
- calculating blood volume in the organ as a quotient of the injected indicator concentration with reference to the organ tissue and the injected indicator concentration with reference to the blood volume in the organ; and
- calculating the blood flow in the organ as a quotient of the blood volume in the organ and the mean transit time mtt when the stop criterion has been reached.

In contrast to the method and device described in *Pfeiffer et al.*, in the device recited in Applicants' claim 1, all values are determined from a single signal measured with a single wavelength at the organ under observation and thus the values obtained are absolute and not relative values. Moreover, only

one light source and one photodetector are required in Applicant's device as recited in claim 1.

In further contrast to the method and device described in *Pfeiffer et al.*, the surge time required to calculate the non-absolute blood flow index according to *Pfeiffer et al.*, is not necessary for the determination of blood flow and blood volume in the device and method recited in Applicants' claims 1 and 13. This feature of Applicants' invention represents a substantial improvement as it avoids the main source of errors in the state of the art. Moreover, the transport function g(t) is needed in *Pfeiffer et al.* to calculate the relative blood volume and blood flow index, whereas the evaluation unit as recited in Applicants' claim 1 calculates the blood volume as a quotient of the injected indicator concentration with reference to the organ tissue and the injected indicator concentration with reference to the blood volume in the organ. The blood flow is calculated as the quotient of the blood volume and the determined mean transit time mtt.

The Examiner has taken the position that the arterial a(t) and cerebral c(t) dye curve described in *Pfeiffer et al.*

correspond to the inflow function i(t) and the outflow function o(t), respectively, as defined by Applicants. The Examiner has further taken the position that the transport function g(t) described in *Pfeiffer et al.* corresponds to Applicants' inflow function i(t) because it is g(t) and not a(t) which is iteratively determined according to *Pfeiffer et al.* (See *Pfeiffer et al.* column 5, lines 19) and can be written as a sum (See *Pfeiffer et al.* column 5, line 52). Accordingly, it is respectfully submitted that the Examiner's conclusion is in error, as the the Examiner has related one function recited in Applicants' claim 1, namely a(t), to two functions in *Pfeiffer et al.*, namely a(t) and g(t). Furthermore the outflow function o(t) is not a measured signal in the device as recited in Applicants' claim 1 as is c(t) in *Pfeiffer et al.*

Claim 2 as amended incorporates the subject matter of claim 1 and further recites the *"scaling of the inflow function i(t) by means of values determined from the pulsatile component of the input signal"*.

Pfeiffer et al. fails to teach or suggest the device aa recited in Applicants' claim 2 for at least the same reasons set

forth above with respect to claim 1. Moreover, the Examiner has taken the position that in *Pfeiffer et al.*, the auxiliary variable of the integral provides a scaling factor (See *Pfeiffer et al.*, column 5, line 10-11). This would imply that the solution of the convolution integral is dependent on the choice of the auxiliary variable; however this relationship is in contradiction to the mathematical theory of convolution integrals. Thus, *Pfeiffer et al.* fails to explicitly or implicity teach or disclose a scaling factor as recited in Applicants' claim 2.

Applicants' method claims 13 and 14 recite the steps as recited in claims 1 and 2 respectively, and accordingly it is respectfully submitted that *Pfeiffer et al.* fails to teach or suggest Applicants' method as recited in claims 13 and 14 for at least the reasons set forth above with respect to claims 1 and 2.

Chen (US 6,339,714) discloses an alternative measurement set up with one light source (14) and two photodetectors (15, 16) for determining the arterial and cerebral dye curves. The pulsatile and non-pulsetile components of the detected signal of the near

photodetector (15) according to *Chen* are divided by each other to determine the attenuation OD_a caused purely by the arterial blood and hence the arterial dye curve. The other photodetector (16) is required in *Chen* to measure the attenuation of the light OD_b, which passes through the brain.

The device and method as recited in Applicants' claims 1 and 13 differs from *Chen* in that Applicant's device and method require only one source and one detector to determine the same information. Moreover, as recited in Applicants' claims 1 and 13, the injected indicator concentration with reference to the blood volume in the organ is determined from the pulsatile component of the input signal and the iteratively determined inflow function i(t). Thus, the pulsatile and non-pulsatile components of the signal are used differently in *Chen* and in Applicants' claimed invention. *Chen* also fails to teach or suggest any determination procedure or device to determine an organ blood volume or an organ blood flow.

The primary differences between *Pfeiffer et al.* and Applicants' pending claims are manifest in the measurement of only a single signal and the determination procedure of the organ

blood flow and organ blood volume as recited in Applicants' claims. Thus for the reasons set forth above, *Pfeiffer et al.* in view of *Chen* does not render Applicants' claims obvious.

It is respectfully submitted the cited references, either alone or in combination, fail to disclose or suggest the device and method as recited in Applicants' pending claims and furthermore fail to teach the benefits that result from the device and method as recited in Applicants' claims which include:

- the measuring of a single signal with respect to the organ under observation;
- the determination of organ blood flow and blood volume with respect to the organ under observation from the single signal;
- the ability to cancel all scattering and reflecting losses since the measured values are absolute because they are determined form a single signal;
- the reduction in the number of light sources and photodetectors; and
- the elimination of the error of determining surge time in the obtained values.

Accordingly, it is respectfully submitted that the claims are patentable over the cited references.

The Commissioner is hereby authorized to charge the undersigned's Deposit Account No. 03-2468 in the amount of $210.00 representing the official fee for one (1) independent claim in excess of three (3) in the application.

In summary, claims 2 and 14 have been amended. In view of the foregoing, it is respectfully requested that the claims be allowed and that this application be passed to issue.

Respectfully submitted,
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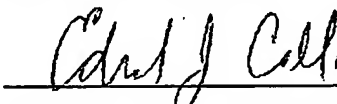

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I hereby certify that this correspondence is being sent by facsimile-transmission to Examiner Amanda L. Lauritzen, Group 3737, United States Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450 on **January 9, 2008**.

Edward J. Callaghan

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